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ST. ONGE STEWARD JOHNSTON & REENS, LLC
986 BEDFORD STREET
STAMFORD, CT 06905-5619

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RECORD OF ORAL HEARING

U. S. PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte NICHOLAS V. PERRICONE and CHIM POTINI

Appeal 2010-004708 and 2010-005507
Application 10/750,390 and 11/506,137
Technology Center 1600

Oral Hearing Held: May 5, 2011

Before DEMETRA J. MILLS, RICHARD M. LEBOVITZ and MELANIE L. MCCOLLUM, *Administrative Patent Judges*

ON BEHALF OF THE APPELLANT:

STEPHEN P. MCNAMARA, ESQ.
986 Bedford Street
Stamford, Connecticut 06905-5619

The above-entitled matter came on for hearing on Thursday, May 5, 2011, commencing at 9:35 a.m., at the U.S. Patent and Trademark Office, 600 Dulany Street, 9th Floor, Hearing Room B, Alexandria, Virginia, before Lori B. Allen, notary public.

THE USHER: Appeal Number 2010-004708, Mr. McNamara.

JUDGE MILLS: Mr. McNamara, do you have a business card for the court reporter?

MR. MCNAMARA: I do.

JUDGE MILLS: Okay. We are familiar with the record in both of the cases that are before us. And you have 20 minutes and can begin when you're ready.

MR. MCNAMARA: I wanted to discuss both applications somewhat concurrently since there's overlapping subject matter. Since the time of the briefing there was a decision from the board of appeals in some related cases that may impact these particular two applications. I didn't know if you had had a chance to look at those decisions as well, but I would call that to your attention.

The previous panel held that claims in issue in the two prior pending applications were potentially indefinite with respect to the claim language. Non liposomal multilamellar liquid crystal phosphatidyl cooling non-pored carrier. And so that decision may impact the claims that are in issue in one of the two applications, not in the second one. It's irrelevant, potentially, to the '390 application.

JUDGE MILLS: Do you happen to have the serial number for that case?

MR. MCNAMARA: There are two sort of very similar decisions, but the decisions were in 11,334,442. That's Appeal Number 2009-014,845. And, also a similar decision issued in Serial Number 11, 334,206,

and that was Appeal Number 2009-010,848. So as I said, that decision may have some relevance to one of these two applications where the board said that that claim language that was an issue was indefinite because it was unclear to the board what were the necessary components to arrive at the claimed composition -- that it was a mixture of ingredients. And so it was unclear what were the essential elements of that.

MR. MCNAMARA: They were refilled with amended claims. There was further rejection, final rejection, continuation in one, so it's still with the examiner in prosecution.

JUDGE LEBOVITZ: Okay.

MR. MCNAMARA: Those two appeal decisions also do address a couple of the 112 issues that are in issue in the '390 application. In the prior decision the board indicated that with respect to the written description objection of the examiner essentially that that objection was moot because the claims were amended so that the objection to return non-pore phosphatidyl cooling wasn't really applicable because the claims now said "nonpolar carrier." The same issue is applicable here in the '390 application, and so that might be some guidance on that issue.

As I said, the second 112 issue in the prior appeal was this question of non-polar phosphatidyl cooling being indefinite, and so the board didn't really address that one way or another previously, but instead substituted its own new indefiniteness rejection, and basically did not adopt the examiner's rejection. So that may impact the '390 application at issue here, particularly Claim 1 has some of the same language that was felt to be indefinite by the prior panel.

I would argue that Claims 2 and other dependent claims that claim from Claim 1 have a lot more specificity in the context of the concern of the board, the prior panel, that what this term meant was --

JUDGE LEBOVITZ: Well, let us read the decision so we understand what the issue is.

MR. MCNAMARA: Okay.

JUDGE LEBOVITZ: Do you want to distinguish now why a multilamellar liquid crystal with phosphatidylcholine is a non liposome? Because liposomes are typically multilamellar, why is a multilamellar composition which has phosphatidylcholine in it non-liposome? Where is the support for that in the spec? That seems to be one of the examiner's problems.

MR. MCNAMARA: Yes, I view this as an issue of what is a person of ordinary skill going to interpret this language to mean.

JUDGE LEBOVITZ: Yes.

MR. MCNAMARA: And, you know, in the field of liquid crystals there are a range of crystal structures that have particular labels that are known to people who are experts in that field.

JUDGE LEBOVITZ: But do we have any expert testimony here?

MR. MCNAMARA: No, but we do have a variety of articles that have been cited in the record, both by the examiner and by the applicant.

JUDGE MILLS: We're familiar with Esposito and its description of several different micelle phases, but Esposito doesn't appear to get to the distinction of liquid crystals being non-polar and also doesn't specifically indicate that they're non lipothermal.

MR. MCNAMARA: I think the non-polar issue is at this point unfortunate in view of the prior panel decision, and that on remand I'm going to be removing the language I did in the other cases, because I think it adds nothing other than confusion to the discussion. And the point that the applicant is trying to define is the notion of the physical structure of the particular claim composition is one of these multilamellar stacks as opposed to spherical structures, so clearly very distinct structures. And, you know, the question is what does -- how should we interpret the claim as it's presented.

JUDGE LEBOVITZ: Okay. So that is understandable that by non-liposome you mean a non-vesicular multilamellar structure, but is there support in the specification for that or is there an argument that that would just be inherent somehow to what was made?

MR. MCNAMARA: I think there is support in the specification that I think it's page 4, paragraph 13. Let me see if I can find that. No. Where the specification says the stabilizing compositions may be in liquid crystal phase with the phosphatidylcholine loosely arranged in multilamellar fashion with polypeptide or macromolecule being bonded and entrapped within the bilayers formed therein. This forms a loosely arranged, yet stable PPC-enriched phosphatidyl cooling insulin complex, and so it doesn't. You know.

In the specification it's written it doesn't really contemplate all the range of potential liquid crystal structures, but it was intended to be this notion of a stack of a series of layers that are sliding one on top of each other, as opposed to something that, you know, peals off and becomes a liposome, which in the crystal world it was very much dependent on the amount of lipid

versus the aqueous solution, temperature, energy, input into the mixture.

What particular structure you get is very dependent on the range of conditions? In this particular case the applicant was focusing on a particular physical structure of stacks, which arrives at through the particular combination of ingredients as well as the process of putting together, particularly there's a described example. There's a long cooling process where it's swept for -- I can't remember how long . It's 12 hours of something.

That allows you to end up with this particular liquid structure which is stacks as opposed to vesicles of some sort. So the issue then in both of these appeals is, you know, what does multilamellar and liquid crystal mean. Does it mean stacks as the applicant intended, or should it be read more broadly to encompass objects such as liposomes that may have multiple layers, but which are not stacks? And, you know, do I have a problem adding the word "stack" in as a new matter. It was not intended to be a liposome, but, you know, the wording was clearly intended to be on this sort of facts as opposed to something --

JUDGE MILLS: So you have stacks of lipid bilayers?

MR. MCNAMARA: Correct.

JUDGE MILLS: So that you still have the lipid bilayer language.,

MR. MCNAMARA: I think the language is multilamellar liquid crystal and I think that that language does not read on liposomes, at least to a person of ordinary skill in the art, because there are all these range of different cubic phases, multilamellar phases. A lamellar phase is a distinct phase from a cubic phase, and a cubic phase is often a particular phase.

JUDGE MCCOLLUM: Is there anything in the record you can point to that would explain that to us?

MR. MCNAMARA: There is the Esposito article that's in the "Evidence" Appendix. There is in the second appeal, the '137 application, the examiner has cited to a couple of articles; one by Rawat, R-a-w-a-t, 2007 article after the application filing that illustrates different types of --

JUDGE LEBOVITZ: Right. And if you look at, I think, I'm not quite sure why the evidence should be different in these two cases.

MR. MCNAMARA: Well there's different rejections based on different art.

JUDGE LEBOVITZ: Right. But I assume the issues are similar, especially with the Rawat one. But didn't that one talk about -- it seemed absolutely to say that you have liquid crystal bilayer stacks, and then when you add water to it, then you get the liposomes.

MR. MCNAMARA: That was one of those two articles. I think it was, probably Berkenstahl, or it could have been Rawat; but whichever one it was, that is describing the process of making the liposome in the sense that you hydrate the lipid stack and keep adding aqueous solution to it.

JUDGE LEBOVITZ: Yes.

MR. MCNAMARA: It begins to puff up and you add energy to it either by stirring it or ultrasonically, and these layers peel off and form vesicles.

JUDGE LEBOVITZ: Yeah.

MR. MCNAMARA: But basically that's an unstable stack at that point in time, because it wants to go into a liposomal form and it takes a little

bit of a nudge sometimes.

JUDGE LEBOVITZ: Yeah. But maybe we're jumping around a little and I'm not sure how this plays out, but Rawat says Liposomes are formed with thin lipid films or lipid takes are hydrated and stacks of liquid crystal bilayers become fluid and swell. So the examiner, I think, had that backwards, because what this sentence says to me is that you have stacks of liquid, crystal bilayers, and when you add water to it then they become liposomes. That's what that sentence says to me.

MR. MCNAMARA: I agree with your understanding, and that's correct. You can make a liposome by having a higher aqueous content relative to your lipid content.

JUDGE LEBOVITZ: Right. Right. And I mean it's not of record here, but whether you get those liposomes formed may depend upon how you add the water, how much water you add and those kinds of conditions.

MR. MCNAMARA: That's correct. That's correct. And the second aspect of the claims that are here before us is the claim indicates a certain degree of stability, the ability to stabilize influandum or another polypeptide at room temperature for a significant period of time. And that stability aspect of it, which is why it's so interesting is particularly as a topical insulin product for someplace like Africa or Asia without refrigeration. That's why this is really, really interesting.

That stability aspect is part of the claim, and I think that stability is not seen in the example, for example, in the Rawat article where it's talking about hydrating things and these sheets peel off and form liposomes. That's

not a stable composition such as intended by this particular crystal form that's called for in the claims. What we have here, I think, is a case like -- well, let me jump back. The examiner sort of has argued, well, if it's the same molecule, it doesn't matter, you know.

If it's phosphatidylcholine here and it's phosphatidyl choline in the prior art, isn't that the same thing? And I would say no. There's plenty of examples where we know of where that is a very simplistic analysis and it's not the last word on the issue. We can have D&L isomers of the exact same molecule, one that's highly bioactive and one that's poisonous. It's the exact same molecule, you know, but what happens to be an optical isomer of the other, and they have completely different properties? That's because they have different physical structures.

In the same way there's lots of prescription drugs that come in different crystal polymorphs; again, the same issues with the higher efficacy in one polymorph as opposed to the other. Structure makes a difference in biological activity in the same way structure makes a difference in the particular application of this technology. And here we're trying to specify these stacks of phosphatidylcholine and trapping layers of polypeptide to allow a stable product that allows transport through the skin of the active ingredient in some way. And so just to say that something is phosphatidylcholine in the prior art example doesn't tell us anything about whether or not the present invention is or is not obvious.

JUDGE MCCOLLUM: Didn't the prior art Anselem disclose liquid crystal structures of phosphatidylcholine?

MR. MCNAMARA: I think it does. It does talk about different

-- Anselem, which I remember. You know. It's a particle surrounded by layers of phosphatidylcholine in the shell. So it's like some kind of particle, but it doesn't really discuss as a recall any stack kind of approach to formulation.

JUDGE LEBOVITZ: But that was the article talking about feeling emulsions.

MR. MCNAMARA: Yes, and that is somewhat like other types of spherical particles that are hollow; but this one happens to have a solid core on the inside. And I don't remember anything else that addresses your question, particularly, at this point.

JUDGE LEBOVITZ: Because that one, it seems to say that emulsuls have the characteristics of liposomes and emulsions; but, it also says that the lipids have liquid crystal phases. The structure of that composition was a little unclear whether it's made up of some particles that are spheres that are micells or liposomes, and some which are just particles of stacks of layers.

MR. MCNAMARA: Yeah. I agree with you. It's a little unclear exactly what it is, but let me at least throw out this additional thought here. You know. All of these prior art references again focus on some type of spherical construct of some sort, and there's in part a reason for that, which is that gives you the maximum drug dosage. You know. In a spherical delivery, as opposed to something like the present invention which requires a more diffuse content of the active ingredient within the lipid layers.

And so in a sense if you're trying to enhance your delivery mechanism, a person of ordinary skill in the art might think that something

that has a spherical structure with some sort of vesicle structure is going to be more effective than a stacked structure. And so from a perspective of teaching away, an old resort seems to be directed at this vesicle structure. And that may be the reason for it. I don't know why.

There's certainly nothing in the art that's directed using a stack structure as a lipid-based carrier. Even the Rawat article, which we were just discussing, talks about and which is subsequent to the filing of this application, talks about potential lipid-based carrier systems from a controlled delivery of peptides and proteins are liposomes, solid lipid and nanoparticles, oily suspensions, submicron lipid emulsions, lipid implants, microtubials, microbubbles, microspheres, but not just a plain stack of a plain liquid, crystal multilamellar structure.

JUDGE LEBOVITZ: Well, where does the specification support that? Can you even show me where the specification talks about liquid crystals, or just liquid crystal phase?

MR. MCNAMARA: I think it's page 4, paragraph 13.

JUDGE LEBOVITZ: And which application?

MR. MCNAMARA: It should be the same book. It's the same specification.

JUDGE MILLS: I didn't notice --

JUDGE LEBOVITZ: Is it the same application, different claim? I'm having trouble finding that.

MR. MCNAMARA: Page 4, paragraph 13 in the '390 application. This is page 4, right before 14.

JUDGE LEBOVITZ: Yeah.

MR. MCNAMARA: It's in a "liquid crystal phase, loosely arranged, multilamellar fashion."

JUDGE LEBOVITZ: Oh. Okay. Yeah. Thank you.

MR. MCNAMARA: And it also appears on page 5, paragraph 14.

JUDGE LEBOVITZ: And it's "entrapped within the liquid bilayer," so I suppose that -- and I'm just thinking out loud -- in a normal liposome you would say it's in the core, the center. But, here, it says it's entrapped within the liquid bilayer,

MR. MCNAMARA: That's correct. And between the layers and sheets of the stack, which flowed upon each other. And you're correct that a liposomal structure has a large cavity in the center where you're active ingredient would reside and be delivered into --

JUDGE MCCOLLUM: Can I just focus in on the claim of the '390? I just want to make sure. Obviously, you're relying on the words "non liposome" to distinguish?

MR. MCNAMARA: That's correct.

JUDGE MCCOLLUM: Is there any other words in this claim that I should be focusing on as distinguishing?

MR. MCNAMARA: The original as drafted we used the word "multilamellar liquid crystal" to try and distinguish from -- you know, to specify -- to say what it is, we added the language "non liposomal" in an effort to respond to rejections to distinguish from the liposomal to make it very clear that this is stacks and not liposomes.

JUDGE MCCOLLUM: Okay.

MR. MCNAMARA: So that's in the '390 application, but it's not in the other application.

JUDGE MCCOLLUM: So it's also your position that the words "multilamellar liquid crystal" in the art means stacks?

MR. MCNAMARA: Yes.

JUDGE MCCOLLUM: And, okay.

JUDGE MILLS: It seems like the claim might have been clear just for your continued prosecution if you specified that the insulin is entrapped between the lipid bilayers that might be an approach to take it seems might be helpful.

MR. MCNAMARA: Thank you. I appreciate that, but I think the issues are pretty much what we've just covered. It's down to a claimed construction; what is multilamellar crystal mean. Does it mean just stacks, or does it mean anything that might have some kind of layers, which require some thought about what does it mean to a person of ordinary skill in the art based on the references of record.

And if you conclude, well, you know, a person of ordinary skill in the art would think this means stacks. I think all this prior art is irrelevant. If it may mean something broader, then yes. Then the examiner's rejection gets sustained and I have to go and figure a way to define what I'm trying to define, which are the stacks in a way that distinguishes from the prior art.

JUDGE MILLS: Did you have any specific comments about the design or the Modiate reference, or just your general comment?

MR. MCNAMARA: I think the briefing covers that in the details that need to be covered, because I think it's really the central claim

construction issues that governs whatever the outcome's going to be here. I thank you very much for your attention.

JUDGE MILLS: Okay. Very good. Thank you.

(Whereupon, at 10:09 a.m., the proceedings were concluded.)